Clinical Update

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Periodontal medicine, part I: periodontal disease as a risk factor in pre-term low birth weight babies

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Introduction

While infant mortality rates have declined in past years, the incidence of low birth weight and preterm infants has increased to over 500,000 newborns per year and remains a significant cause of perinatal morbidity and mortality. Approximately 60% of infant mortalities with no associated congenital defects are directly attributable to Preterm Low Birth Weight (PLBW), which is defined as infants <5.5 lbs. or <37 week gestation.[1] Factors which have a positive correlation with an increased risk of PLBW include: mother's age (<17 or > 34), socioeconomic status, bacterial vaginosis, inadequate prenatal care, drug and alcohol abuse, smoking, malnutrition, diabetes, high blood pressure, multiple pregnancies, and systemic maternal infections, which includes periodontal disease.[2] The purpose of this clinical update is to review the relationship between periodontal disease and PLBW.

What effect does oral bacteria have on the fetus?

During a normal pregnancy production of prostaglandin, specifically prostaglandin E-2 (PGE-2) in the amnion, gradually increases throughout gestation. When levels of PGE-2 reach a threshold level, labor is induced followed by delivery.[3]

Recently, an association between infection and PLBW has been demonstrated, with common inflammatory pathways mediating the development of PLBW. During an infection researchers noted a consistent increase in PGE-2, Tumor Necrosis Factor (TNF), and Interleukin 1 (IL-1). Interleukin 6 (IL-6) has also been positively correlated with the incidence of PLBW. Evidence indicates the potential mechanism of these cytokines as biochemical mediators of preterm labor. For example, Bacterial Vaginosis (BV) is a vaginal infection and is one of the most common factors associated with PLBW. The primary mechanism by which PLBW occurs could be due to an ascending infection from the vagina and endocervix.[4] Gram-negative bacteria associated with this condition produce endotoxins and enzymes that stimulate pro-inflammatory cytokine production, which results in increased levels of TNF, IL-1, IL-6, and PGE2.[5] Treatment of this infection with antibiotics has successfully decreased the rate of PLBW.

In a similar mechanism, intra-oral bacteria such as F. Nucleatum potenially influence the distant fetus via a hematogenous route.[5] *F. Nucleatum* and *Camphylobacter* are periodontal pathogens that have a higher prevalence in patients with periodontal disease. These bacteria, indigenous to the oral cavity, have also been cultured from the amniotic fluid of preterm mothers and have been implicated in PLBW. It has been found that species and subspecies of *F. nucleatum* isolated from the amniotic fluid of women with preterm labor more closely matched those strains found in subgingival plaque than strains from the lower genital tract.[5] These findings have led researches to conclude that most premature birth cases are probably caused by infections of unknown origin.

Can periodontal disease cause PLBW?

Periodontal infections during pregnancy may increase bacterial products in the amniotic fluid such as lipopolysaccharide (LPS) and enzymes from gram-negative bacteria, which in turn stimulates the production of host derived cytokines. These cytokines, including IL-1, TNF, and IL-6, stimulate increased production of PGE-2 leading to the onset of preterm labor. This premature rise in PGE-2 is characteristic of preterm labor, regardless of whether the infection is detected. Therefore, the gram-negative bacteria from a periodontal infection may have a distant effect by increasing the PGE-2 to sufficient levels to induce premature labor and pose a threat to the fetal placenta.[6]

Several studies recently published have investigated this relationship between periodontal disease and PLBW. In a 1996 study of 124 pregnant women, Offenbacher found that those women with severe periodontal disease had a 7.5 fold increased risk of preterm birth, which was a greater risk factor than either alcohol or smoking.[7] In a similar study, Jeffcoat et al. compared 1,313 pregnant women and found that the risk of preterm birth in women with generalized periodontitis was 4 to 7 times higher than in patients with no disease.[8] Offenbacher, evaluating this relationship in an animal study, found that PGE2 and TNF were both increased in the amniotic fluid of animals with periodontitis compared to those without periodontal disease. There was an almost 4 fold increase in PGE2 in the periodontitis group.[7]

In a cross sectional study, women having LBW infants had significantly higher levels of periodontal pathogens (A. actinomycetocomitans, B. Forsythus, P. Gingivalis, and T. Denticola) in their subgingival plaque than women who had normal birth weight babies.[7] Women having PLBW also had

higher levels of gingival crevicular fluid with PGE and IL-1, and these levels were inversely related to their infants' birth weight. Thus, women with higher PGE in the gingival crevicular fluid had smaller and more premature infants. Gingival crevicular fluid levels of PGE-2 and IL-1 have been shown to highly correlate with amniotic levels of each.[7]

Can periodontal therapy reduce the incidence of PLBW?

In 2002, Lopez et al. found that women treated by scaling/root planing during pregnancy had a preterm birth incidence of <2% while those treated after delivery had a preterm birth incidence of 10%.[9] In an intervention study, Jeffcoat et al. provided non-surgical periodontal therapy to pregnant women at 21-24 weeks gestation and compared the results to women receiving no therapy. The untreated group had a preterm birth rate of 6% compared to the treated group which had a preterm birth rate of 0.8%. It has been estimated that 18% of all cases of PLBW may be due to periodontal infections, making it a clinically important risk factor for PLBW.[8]

Pregnant women with periodontitis may have an increased risk to PLBW. Dental treatment should include a periodontal examination, oral hygiene instruction, and a thorough cleaning. Likewise, a hygiene recall schedule should be established until delivery. All women of childbearing age should have a dental/periodontal examination and periodontal health should be established as well as maintained.

The data from these studies support the hypothesis that untreated periodontal disease increases the risk for PLBW. If conventional periodontal therapy does reduce the risk of preterm birth, then it will need to be determined which mode of treatment is most efficacious and cost effective.[10]

Conclusion

PLBW is a multi-factorial development and establishing direct correlation with any risk factor is a complex undertaking. Most of the literature to date suggests a positive correlation between periodontal disease and PLBW. The association between periodontal disease and PLBW is supported by epidemiological data, experimental studies, and documentation of maternal and fetal host responses to periodontal bacteria.[11] If ongoing studies show that treatment of periodontal infections substantially reduces the risk of adverse pregnancy outcomes, then periodontal therapy should be considered a vital part of prenatal care.

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